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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	BEILSTEIN updated with new compounds
NEWS 12	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 13	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 14	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 15	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 16	AUG 27	USPATOLD now available on STN
NEWS 17	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 18	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 19	SEP 13	FORIS renamed to SOFIS
NEWS 20	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 21	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 22	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 23	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 24	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 00:17:06 ON 11 OCT 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 9 OCT 2007 HIGHEST RN 949922-95-6
DICTIONARY FILE UPDATES: 9 OCT 2007 HIGHEST RN 949922-95-6

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http://www.cas.org/support/stngen/stndoc/properties.html

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.45	0.66

FILE 'HCAPLUS' ENTERED AT 00:17:20 ON 11 OCT 2007
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FILE COVERS 1907 - 11 Oct 2007 VOL 147 ISS 16

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FILE LAST UPDATED: 10 Oct 2007  (20071010/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s antranilic () acid () amide?
             9 ANTRANILIC
       4457643 ACID
       1595800 ACIDS
       4961115 ACID
                 (ACID OR ACIDS)
        181128 AMIDE?
L1           0 ANTRANILIC (W) ACID (W) AMIDE?

=> s anthranilic () acid () amide?
         12520 ANTHRANILIC
             1 ANTHRANILICS
         12520 ANTHRANILIC
                 (ANTHRANILIC OR ANTHRANILICS)
       4457643 ACID
       1595800 ACIDS
       4961115 ACID
                 (ACID OR ACIDS)
        181128 AMIDE?
L2          67 ANTHRANILIC (W) ACID (W) AMIDE?

=> s l2 and VEGF () inhibitor?
         21171 VEGF
           182 VEGFS
         21189 VEGF
                 (VEGF OR VEGFS)
       1063541 INHIBITOR?
           258 VEGF (W) INHIBITOR?
L3           1 L2 AND VEGF (W) INHIBITOR?

=> s l3 and review/dt
       2076262 REVIEW/DT
L4           0 L3 AND REVIEW/DT

=> d l3, ibib abs hitstr, 1

L3   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:283363  HCAPLUS
DOCUMENT NUMBER:          142:329832
TITLE:                    Combination of a vegf receptor inhibitor with a
                          chemotherapeutic agent
INVENTOR(S):              Bold, Guido; Brueggen, Josef Bernhard; Huang, Jerry
                          Min-Jian; Kinder, Frederick Ray, Jr.; Lane, Heidi;
                          Latour, Elisabeth Jeanne; Manley, Paul William; Wood,
                          Jeanette Marjorie
PATENT ASSIGNEE(S):       Novartis Ag, Switz.; Novartis Pharma GmbH
SOURCE:                   PCT Int. Appl., 71 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE


Updated Search
```

WO 2005027972	A2	20050331	WO 2004-EP10686	20040923
WO 2005027972	A3	20051103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004273615	A1	20050331	AU 2004-273615	20040923
CA 2537991	A1	20050331	CA 2004-2537991	20040923
EP 1682181	A2	20060726	EP 2004-765542	20040923

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

CN 1856327	A	20061101	CN 2004-80027544	20040923
BR 2004014698	A	20061128	BR 2004-14698	20040923
JP 2007505938	T	20070315	JP 2006-527348	20040923
MX 2006PA03163	A	20060605	MX 2006-PA3163	20060320
IN 2006CN00982	A	20070615	IN 2006-CN982	20060322
NO 2006001777	A	20060623	NO 2006-1777	20060421
PRIORITY APPLN. INFO.:			US 2003-505250P P	20030923
			WO 2004-EP10686 W	20040923

OTHER SOURCE(S): MARPAT 142:329832

AB The present invention relates to a combination therapy for treating patients suffering from proliferative diseases or diseases associated with persistent angiogenesis. The patient is treated with: (a) a VEGF inhibitor compound; and (b) one or more chemotherapeutic agents selected from the group consisting of: an aromatase inhibitor; an anti-estrogen, an anti-androgen (especially in the case of prostate cancer) or a gonadorelin agonist; a topoisomerase I inhibitor or a topoisomerase II inhibitor; a microtubule active agent, an alkylating agent, an anti-neoplastic anti-metabolite or a platin compound; a compound targeting/decreasing a protein or lipid kinase activity or a protein or lipid phosphatase activity, a further anti-angiogenic compound or a compound which induces cell differentiation processes. The patient is treated with :(a) a VEGF inhibitor compound;and (b) one or more chemotherapeutic agents selected from the group consisting of : a bradykinin 1 receptor or an angiotensin II antagonist ; a cyclooxygenase inhibitor , a bisphosphonate , a heparanase inhibitor (prevents heparan sulfate degradation) , e.g. , PI-88 , a biol. response modifier, preferably a lymphokine or interferons , e.g., interferon γ, an ubiquitination inhibitor, or an inhibitor which blocks anti-apoptotic pathways ; an inhibitor of Ras oncogenic isoforms or a farnesyl transferase inhibitor ; a telomerase inhibitor , e.g. , telomestatin ; a protease inhibitor, a matrix metalloproteinase inhibitor , a methionine aminopeptidase inhibitor , e.g. , bengamide or a derivative thereof , or a proteasome inhibitor , e. g. , PS-341. The patient is treated with : (a) a VEGF inhibitor compound (b) one or more chemotherapeutic agents selected from the group consisting of : agents used in the treatment of hematol. malignancies or FMS-like tyrosine kinase inhibitors ; an HSP90 inhibitors ; HDAC inhibitors ; mTOR inhibitors ; somatostatin receptor antagonists ; integrin antagonists ; anti-leukemic compds. ; tumor cell damaging approaches such as ionizing radiation EDG binders ; anthranilic acid amide class of kinase inhibitors ; ribonucleotide reductase inhibitors ; S-adenosylmethionine decarboxylase inhibitors ;

antibodies against VEGF or VEGFR ; photodynamic therapy ; angiostatic steroids ; implants containing corticosteroids ; AT1 receptor antagonists ; ACE inhibitors.

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=> d his

     (FILE 'HOME' ENTERED AT 00:17:06 ON 11 OCT 2007)

     FILE 'REGISTRY' ENTERED AT 00:17:15 ON 11 OCT 2007

     FILE 'HCAPLUS' ENTERED AT 00:17:20 ON 11 OCT 2007
L1             0 S ANTRANILIC () ACID () AMIDE?
L2            67 S ANTHRANILIC () ACID () AMIDE?
L3             1 S L2 AND VEGF () INHIBITOR?
L4             0 S L3 AND REVIEW/DT

=> s VEGF () inhibitor?
          21171 VEGF
            182 VEGFS
          21189 VEGF
                (VEGF OR VEGFS)
        1063541 INHIBITOR?
L5          258 VEGF (W) INHIBITOR?

=> s l5 and neoplastic () disease?
          61232 NEOPLASTIC
             19 NEOPLASTICS
          61246 NEOPLASTIC
                (NEOPLASTIC OR NEOPLASTICS)
        1125002 DISEASE?
           2437 NEOPLASTIC (W) DISEASE?
L6             1 L5 AND NEOPLASTIC (W) DISEASE?

=> d l6, ibib abs hitstr, 1

L6   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:542305  HCAPLUS
DOCUMENT NUMBER:          145:34209
TITLE:                    Antitumor combinations containing a VEGF
                          inhibitor and 5-FU or one of its derivatives
INVENTOR(S):              Vrignaud, Patricia; Chiron-Blondel, Marielle; Bissery,
                          Marie-Christine; Furfine, Eric; Holash, Jocelyn;
                          Cedarbaum, Jesse M.
PATENT ASSIGNEE(S):       Aventis Pharma S.A., Fr.
SOURCE:                   PCT Int. Appl., 16 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2006059012         A1    20060608    WO 2005-FR3005          20051202
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
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Updated Search

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            VN, YU, ZA, ZM, ZW
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
            IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
            CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
            GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM
     FR 2878749           A1    20060609    FR 2004-12870          20041203
     AU 2005311191        A1    20060608    AU 2005-311191         20051202
     CA 2586735           A1    20060608    CA 2005-2586735        20051202
     US 2006178305        A1    20060810    US 2005-293761         20051202
     EP 1824504           A1    20070829    EP 2005-824581         20051202
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
             BA, HR, MK, YU
     IN 2007KN01868       A     20070810    IN 2007-KN1868         20070524
PRIORITY APPLN. INFO.:                     FR 2004-12870       A  20041203
                                           WO 2005-FR3005      W  20051202
AB   An antitumor composition contains a VEGF inhibitor and a
     5-fluorouracil or a 5-fluropyrimidine derivs. for the treatment of
     neoplastic diseases.  A s.c. injection contained VEGF 25
     mg diluted in 1 mL phosphate buffer.  An i.v. injection contained 5-FU diluted
     with 5 mL of 5% glucose solution  The injection solns. are administered
     simultaneously by perfusion.
REFERENCE COUNT:          11    THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> dh is
DH IS NOT A RECOGNIZED COMMAND
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"HELP COMMANDS" at an arrow prompt (=>).

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     (FILE 'HOME' ENTERED AT 00:17:06 ON 11 OCT 2007)

     FILE 'REGISTRY' ENTERED AT 00:17:15 ON 11 OCT 2007

     FILE 'HCAPLUS' ENTERED AT 00:17:20 ON 11 OCT 2007
L1             0 S ANTRANILIC () ACID () AMIDE?
L2            67 S ANTHRANILIC () ACID () AMIDE?
L3             1 S L2 AND VEGF () INHIBITOR?
L4             0 S L3 AND REVIEW/DT
L5           258 S VEGF () INHIBITOR?
L6             1 S L5 AND NEOPLASTIC () DISEASE?

=> s l5 and retinopathy?
          8732 RETINOPATHY?
L7          45 L5 AND RETINOPATHY?

=> s l7 and review/dt
       2076262 REVIEW/DT
L8          11 L7 AND REVIEW/DT

=> d l8, ibib abs hitstr, 1-11

L8   ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:537355  HCAPLUS
DOCUMENT NUMBER:          147:163184
TITLE:                    Aging and retinal vascular diseases


Updated Search
```

AUTHOR(S): Takagi, Hitoshi
CORPORATE SOURCE: Department of Ophthalmology, Hyogo Prefectural Amagasaki Hospital, Japan
SOURCE: Nippon Ganka Gakkai Zasshi (2007), 111(3), 207-230
CODEN: NGZAA6; ISSN: 0029-0203
PUBLISHER: Nippon Ganka Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review. Ocular vascular diseases such as diabetic retinopathy , retinal vein occlusion and age-related macular degeneration, have become leading causes of severe visual disturbance. Macular edema and serous retinal detachment are associated with abnormal vascular leakage and tractional retinal detachment and neovascular glaucoma is caused by retinal neovascularization. Such ocular vascular diseases are caused by vascular cell aging and vascular damage associated with lifestyle-related diseases including diabetes mellitus, hypertension, hyperlipidemia, and obesity. Along with aging, oxidative stress and phys. stress induce apoptosis by intracellular signaling through stress kinases in cultured retinal vascular cells. The inhibition of such stress kinases could be an effective treatment to protect the vascular cells against age related damage. In a retinal vascular developmental model, pericyte loss causes pathol. mimicking macular edema and proliferative diabetic retinopathy. Angiopoietin 1 (Ang I) secreted by pericytes suppresses oxidative stress-induced intracellular signaling through stress kinases linked to cell apoptosis and normalizes such retinal pathol. Ang 1-triggered intracellular signaling is useful for the treatment of vascular cell pathol. associated with pericyte loss. In diabetic retinopathy and retinal vein occlusion,vascular endothelial growth factor (VEGF) has been recognized as a predominant factor to induce the ischemic retinal neovascularization. Neuropillin 1 (NRP 1), which enhances receptor function, is abundantly expressed in the retinal endothelial cells and is upregulated by VEGF and by hypoxia to regulate a pos. feedback mechanism in retinal neovascularization. This receptor could be a unique target for retina-specific therapy. In lifestyle-related diseases which increase along with aging, the renin-angiotensin system which regulates hypertension and cardiovascular diseases and adipocytokines which are abnormally secreted in obesity act as proangiogenic factors. Regulation of such lifestyle-related disease factors is important for the treatment of retinal vascular diseases. Finally, recent research has found that erythropoietin is an ischemia-induced angiogenic factor that acts independently and as potently as VEGF in proliferative diabetic retinopathy (PDR). The VEGF level is particularly high and strongly associated with angiogenic activity in PDR patients. The potential of VEGF inhibitors has recently been recognized in clin. applications. In the present study, the anal. of mol. mechanisms in vascular deficiency using vascular cell biol. methodol. and novel strategies for the treatment of vascular diseases are reviewed with 60 refs.

L8 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:688763 HCAPLUS
DOCUMENT NUMBER: 143:259263
TITLE: Old and new drug targets in Diabetic retinopathy: From biochemical changes to inflammation and neurodegeneration
AUTHOR(S): Leal, E. C.; Santiago, A. R.; Ambrosio, A. F.
CORPORATE SOURCE: Center for Ophthalmology of Coimbra, IBILI, Faculty of Medicine, University of Coimbra, Port.
SOURCE: Current Drug Targets: CNS & Neurological Disorders (2005), 4(4), 421-434
CODEN: CDTCCC; ISSN: 1568-007X

Updated Search

PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Diabetic Retinopathy (DR) is a major complication of diabetes and is a leading cause of blindness in western countries. DR has been considered a microvascular disease, and the blood-retinal barrier breakdown is a hallmark of this disease. The available treatments are scarce and not very effective. Despite the attempts to control blood glucose levels and blood pressure, many diabetic patients are affected by DR, which progresses to more severe forms of disease, where laser photocoagulation therapy is needed. DR has a huge psychol. impact in patients and tremendous economic and social costs. Taking this into account, the scientific community is committed to find a treatment to DR. Understanding the cellular and mol. mechanisms underlying the pathogenesis of DR will facilitate the development of strategies to prevent, or at least to delay the progression of the disease. The involvement of the polyol pathway, advanced glycation end products, protein kinase C and oxidative stress in the pathogenesis of DR is well-documented, and several clin. trials have been conducted to test the efficacy of various drugs. More recent findings also demonstrate that DR has characteristics of chronic inflammatory disease and neurodegenerative disease, which increases the opportunity of intervention at the pharmacol. level. This review presents past and recent evidences demonstrating the involvement of different mols. and processes in DR, and how different approaches and pharmacol. tools have been used to prevent retinal cell dysfunction.
REFERENCE COUNT: 244 THERE ARE 244 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:549365 HCAPLUS
DOCUMENT NUMBER: 143:52831
TITLE: Novel approaches in the treatment of angiogenic eye disease
AUTHOR(S): Wegewitz, U.; Goehring, I.; Spranger, J.
CORPORATE SOURCE: Department of Clinical Nutrition (Chairman Prof. Dr. A.F.H. Pfeiffer), German Institute of Human Nutrition Potsdam-Rehbruecke, Germany
SOURCE: Current Pharmaceutical Design (2005), 11(18), 2311-2330
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Angiogenic eye disease is among the most common causes of blindness worldwide. Current treatment approaches are insufficiently effective and partially associated with significant adverse effects. From an investigational view, the eye provides an ideal setting to observe real-time and serial observations of angiogenesis in vivo in humans. The current understanding of mol. biol. involved in angiogenesis has already led to the identification of a number of potential therapeutic targets, some of them being highly effective angiostatic mols. Most exptl. approaches currently favor or even require the systemic administration of the investigated substances (somatostatin analogs, PKC-inhibitors). However, the systemic administration of bioactive substances always risks significant systemic adverse effects. Due to the morphol. characteristics of the eye, local therapies including intraocular injection or even local gene transfer might be feasible. They might provide a valuable opportunity of targeted and sustained delivery of therapeutic proteins to the retina. This review aims to outline the current understanding of the pathogenesis of proliferative diabetic retinopathy and will

focus on some as yet exptl., but potentially effective new therapeutic possibilities of this disease.

REFERENCE COUNT: 238 THERE ARE 238 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:544265 HCAPLUS
DOCUMENT NUMBER: 143:90112
TITLE: Bevacizumab (Avastin), a humanized anti-VEGF monoclonal antibody for cancer therapy
AUTHOR(S): Ferrara, Napoleone; Hillan, Kenneth J.; Novotny, William
CORPORATE SOURCE: Department of Molecular Oncology, Genentech, Inc., South San Francisco, CA, 94080, USA
SOURCE: Biochemical and Biophysical Research Communications (2005), 333(2), 328-335
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Vascular endothelial growth factor (VEGF) is an endothelial cell-specific mitogen in vitro and an angiogenic inducer in vivo. The tyrosine kinases Flt-1 (VEGFR-1) and Flk-1/KDR (VEGFR-2) are high affinity VEGF receptors. VEGF plays an essential role in developmental angiogenesis and is important also for reproductive and bone angiogenesis. Substantial evidence also implicates VEGF as a mediator of pathol. angiogenesis. Anti-VEGF monoclonal antibodies and other VEGF inhibitors block the growth of several tumor cell lines in nude mice. Clin. trials with VEGF inhibitors in a variety of malignancies are ongoing. Recently, a humanized anti-VEGF monoclonal antibody (bevacizumab; Avastin) has been approved by the FDA as a first-line treatment for metastatic colorectal cancer in combination with chemotherapy. Furthermore, VEGF is implicated in intraocular neovascularization associated with diabetic retinopathy and age-related macular degeneration.
REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:765250 HCAPLUS
DOCUMENT NUMBER: 141:307697
TITLE: Vascular endothelial growth factor: basic science and clinical progress
AUTHOR(S): Ferrara, Napoleone
CORPORATE SOURCE: Department of Molecular Oncology, Genentech, Inc., San Francisco, CA, 94080, USA
SOURCE: Endocrine Reviews (2004), 25(4), 581-611
CODEN: ERVIDP; ISSN: 0163-769X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Vascular endothelial growth factor (VEGF) is an endothelial cell-specific mitogen in vitro and an angiogenic inducer in a variety of in vivo models. Hypoxia has been shown to be a major inducer of VEGF gene transcription. The tyrosine kinases Flt-1 (VEGFR-1) and Flk-1/KDR (VEGFR-2) are high-affinity VEGF receptors. The role of VEGF in developmental angiogenesis is emphasized by the finding that loss of a single VEGF allele results in defective vascularization and early embryonic lethality. VEGF is critical also for reproductive and bone angiogenesis. Substantial evidence also implicates VEGF as a mediator of

pathol. angiogenesis. In situ hybridization studies demonstrate expression of VEGF mRNA in the majority of human tumors. Anti-VEGF monoclonal antibodies and other VEGF inhibitors block the growth of several tumor cell lines in nude mice. Clin. trials with various VEGF inhibitors in a variety of malignancies are ongoing. Very recently, an anti-VEGF monoclonal antibody (bevacizumab; Avastin) has been approved by the Food and Drug Administration as a first-line treatment for metastatic colorectal cancer in combination with chemotherapy. Furthermore, VEGF is implicated in intraocular neovascularization associated with diabetic retinopathy and age-related macular degeneration.

REFERENCE COUNT: 435 THERE ARE 435 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:407599 HCAPLUS
DOCUMENT NUMBER: 141:374331
TITLE: Pharmacological approach to diabetic retinopathy
AUTHOR(S): de la Cruz, Jose Pedro; Gonzalez-Correa, Jose Antonio; Guerrero, Ana; de la Cuesta, Felipe Sanchez
CORPORATE SOURCE: Department of Pharmacology and Therapeutics, School of Medicine, University of Malaga, Malaga, Spain
SOURCE: Diabetes/Metabolism Research and Reviews (2004), 20(2), 91-113
CODEN: DMRRFM; ISSN: 1520-7552
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Diabetic retinopathy is the most frequent cause of legal blindness in the population of 30-to-70-yr olds. Whether retinopathy appears or not depends mainly on the duration of the disease and the degree of metabolic control the patient maintains. High blood glucose values lead to important changes in cellular metabolism and the main effects of these alterations are endothelial dysfunction that sets in motion the morphol. process of diabetic retinopathy. The biochem. lesions caused by prolonged hyperglycemia can be pos. influenced, but usually not normalized, pharmacol. with some groups of drugs, which are now under development. This makes tight control of glycemia a key measure in preventing the onset or progression of diabetic retinopathy, together with an effective program of ophthalmol. detection and follow-up in patients with diabetes. Regarding the role of endothelial dysfunction, antiplatelet drugs have been shown to slow some aspects of the evolution of diabetic retinopathy in its initial stages, mainly a lower degree of microaneurysms. However, a new approach to controlling endothelial dysfunction shows promise, mainly through the vascular endothelial growth factor (VEGF) inhibitors.
These agents may prove to be especially useful in the treatment of proliferative diabetic retinopathy. Other encouraging results have been obtained in studies of antioxidant drugs and inhibitors of the formation of advanced glycation end products. Once retinal lesions appear, preventive measures need to be redoubled, with special attention to controlling glycemia; however, it is also necessary to resort to laser photocoagulation. This intervention aims to eliminate areas of ischemia and to diminish the formation of retinal exudates. If this measure fails or if vitreous hemorrhage appears, the only remaining therapeutic measure is vitrectomy.

REFERENCE COUNT: 246 THERE ARE 246 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L8 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:114750 HCAPLUS
DOCUMENT NUMBER: 140:301189
TITLE: The role of vascular endothelial growth factor (VEGF) in pathogenesis of diabetic retinopathy
AUTHOR(S): Urban, Beata; Peczynska, Jadwiga
CORPORATE SOURCE: Samodzielny Publiczny Dzieciecy Szpital Kliniczny, Klinika Okulistyki Dzieciecej, Akad. Med., Bialystok, 15-274, Pol.
SOURCE: Klinika Oczna (2003), 105(5), 319-321
CODEN: KOAOAE; ISSN: 0023-2157
PUBLISHER: OFTAL Sp. z o.o.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Polish
AB A review. The roles of VEGF in microaneurysm formation, blood-eye retinal barrier breakdown, and development of capillary nonperfusion and retinal neovascularization in the pathogenesis of diabetic retinopathy are discussed. The use of VEGF inhibitors in the treatment of diabetic retinopathy is outlined.

L8 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:105131 HCAPLUS
DOCUMENT NUMBER: 138:284872
TITLE: Biochemical and molecular mechanisms of diabetic retinopathy
AUTHOR(S): Balasubramanyam, M.; Rema, M.; Premanand, C.
CORPORATE SOURCE: Madras Diabetes Research Foundation, Chennai, 600 086, India
SOURCE: Current Science (2002), 83(12), 1506-1514
CODEN: CUSCAM; ISSN: 0011-3891
PUBLISHER: Current Science Association
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Diabetic retinopathy is one of the most common devastating complications of diabetes. Currently there are no accepted drug treatments for diabetic retinopathy and laser therapy is the most accepted treatment option. Biochem. and physiol. changes that occur very early in the retina of diabetic patients are the major signaling determinants of future damage to the retina. However, drug treatment for diabetic retinopathy that will specifically ameliorate biochem. defects, is still only at an exptl. stage. Research during the past few decades has provided ample evidence that hyperglycemia is one of the main factors driving the onset and progression of diabetic retinopathy. Furthermore, hyperglycemia-induced events regulate a variety of cellular signals including the stimulation of growth factors that are implicated in retinopathy. It is possible that in the future, novel therapeutic measures may emerge for the treatment of diabetic retinopathy. To discover anti-permeability and anti-angiogenic compds., a more comprehensive understanding of the mechanisms governing the vascularization of the retina is required. Some of the exptl. approaches currently under investigation, such as protein kinase C inhibitors, VEGF inhibitors, pigment epithelium-derived factor, and many others may prove useful as new therapeutic approaches in the treatment of various stages of diabetic retinopathy. Significant efforts continue to be directed toward the evaluation of the mechanisms underlying diabetic retinopathy to achieve newer and better therapies for this potentially preventable cause of blindness.
REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS

Updated Search

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:657188 HCAPLUS
DOCUMENT NUMBER: 132:45040
TITLE: Molecular and biological properties of vascular endothelial growth factor
AUTHOR(S): Ferrara, Napoleone
CORPORATE SOURCE: Department of Cardiovascular Research, Genentech Inc., South San Francisco, CA, 94080, USA
SOURCE: Journal of Molecular Medicine (Berlin) (1999), 77(7), 527-543
CODEN: JMLME8; ISSN: 0946-2716
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 230 refs. Vascular endothelial growth factor (VEGF) is a fundamental regulator of normal and abnormal angiogenesis. Recent evidence indicates that VEGF is essential for embryonic vasculogenesis and angiogenesis. Furthermore, VEGF is required for the cyclical blood vessel proliferation in the female reproductive tract and for longitudinal bone growth and endochondral bone formation. Substantial exptl. evidence also implicates VEGF in pathol. angiogenesis. Anti-VEGF monoclonal antibodies or other VEGF inhibitors block the growth of many tumor cell lines in nude mice. Furthermore, the concns. of VEGF are elevated in the aqueous and vitreous humors of patients with proliferative retinopathies such as the diabetic retinopathy. In addition, VEGF-induced angiogenesis results in a therapeutic benefit in several animal models of myocardial or limb ischemia. Currently, both therapeutic angiogenesis using recombinant VEGF or VEGF gene transfer and inhibition of VEGF-mediated pathol. angiogenesis are being pursued.
REFERENCE COUNT: 230 THERE ARE 230 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:599354 HCAPLUS
DOCUMENT NUMBER: 132:73677
TITLE: Role of vascular endothelial growth factor in the regulation of angiogenesis
AUTHOR(S): Ferrara, Napoleone
CORPORATE SOURCE: Department of Cardiovascular Research, Genentech, Inc., South San Francisco, CA, USA
SOURCE: Kidney International (1999), 56(3), 794-814
CODEN: KDYIA5; ISSN: 0085-2538
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 285 refs. Compelling evidence indicates that vascular endothelial growth factor (VEGF) is a fundamental regulator of normal and abnormal angiogenesis. The loss of a single VEGF allele results in defective vascularization and early embryonic lethality. VEGF plays also a critical role in kidney development, and its inactivation during early postnatal life results in the suppression of glomerular development and kidney failure. Recent evidence indicates that VEGF is also essential for angiogenesis in the female reproductive tract and for morphogenesis of the epiphyseal growth plate and endochondral bone formation. Substantial exptl. evidence also implicates VEGF in pathol. angiogenesis. Anti-VEGF monoclonal antibodies or other VEGF inhibitors block the growth of several human tumor cell lines in nude mice. Furthermore, the concns. of VEGF are elevated in the aqueous and vitreous humors of

patients with proliferative retinopathies such as the diabetic retinopathy. In addition, VEGF-induced angiogenesis results in a therapeutic benefit in several animal models of myocardial or limb ischemia. Currently, both therapeutic angiogenesis using recombinant VEGF or VEGF gene transfer and inhibition of VEGF-mediated pathol. angiogenesis are being pursued clin.

REFERENCE COUNT: 285 THERE ARE 285 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:457972 HCAPLUS
DOCUMENT NUMBER: 127:75424
TITLE: Suppression of angiogenesis by the inhibition of vascular endothelial growth factor activity
AUTHOR(S): Asano, Makoto; Yukita, Ayako; Suzuki, Hideo
CORPORATE SOURCE: Tsukuba Research Laboratory, Toagosei Co, LTD, Tsukuba, 300-26, Japan
SOURCE: Ganki (1997), 48(4), 443-447
CODEN: GNKIEX; ISSN: 0015-5667
PUBLISHER: Nippon Ganka Kiyokai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 32 refs. Vascular endothelial growth factor (VEGF) is an endothelial cell-selective potent angiogenic factor, inducing the growth of endothelial cells and directly mediating changes in microvascular permeability. Diabetic retinopathy and the growth of solid tumors are known to angiogenic diseases, and according to recent reports, VEGF is highly expressed in the region of these diseases. Because inhibition of the activity of VEGF may inhibit angiogenesis in these diseases, VEGF inhibitors offer a new approach to the treatment of angiogenic diseases. We review here the expression and regulation of VEGF and VEGF inhibitors.

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(FILE 'HOME' ENTERED AT 00:17:06 ON 11 OCT 2007)

FILE 'REGISTRY' ENTERED AT 00:17:15 ON 11 OCT 2007

FILE 'HCAPLUS' ENTERED AT 00:17:20 ON 11 OCT 2007
L1 0 S ANTRANILIC () ACID () AMIDE?
L2 67 S ANTHRANILIC () ACID () AMIDE?
L3 1 S L2 AND VEGF () INHIBITOR?
L4 0 S L3 AND REVIEW/DT
L5 258 S VEGF () INHIBITOR?
L6 1 S L5 AND NEOPLASTIC () DISEASE?
L7 45 S L5 AND RETINOPATHY?
L8 11 S L7 AND REVIEW/DT

=> s l5 and age-related () macula () degeneration?
351777 AGE
60286 AGES
372541 AGE
(AGE OR AGES)
1157218 RELATED
1 RELATEDS
1157219 RELATED
(RELATED OR RELATEDS)
21304 AGE-RELATED

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              12 MACULAS
             164 MACULAE
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                  (MACULA OR MACULAS OR MACULAE)
           54108 DEGENERATION?
              31 AGE-RELATED (W) MACULA (W) DEGENERATION?
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          372541 AGE
                  (AGE OR AGES)
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         1157219 RELATED
                  (RELATED OR RELATEDS)
           21304 AGE-RELATED
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     (FILE 'HOME' ENTERED AT 00:17:06 ON 11 OCT 2007)

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     FILE 'HCAPLUS' ENTERED AT 00:17:20 ON 11 OCT 2007
L1             0 S ANTRANILIC () ACID () AMIDE?
L2            67 S ANTHRANILIC () ACID () AMIDE?
L3             1 S L2 AND VEGF () INHIBITOR?
L4             0 S L3 AND REVIEW/DT
L5           258 S VEGF () INHIBITOR?
L6             1 S L5 AND NEOPLASTIC () DISEASE?
L7            45 S L5 AND RETINOPATHY?
L8            11 S L7 AND REVIEW/DT
L9             0 S L5 AND AGE-RELATED () MACULA () DEGENERATION?
L10           31 S AGE-RELATED () MACULA () DEGENERATION?

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L11            0 L5 AND L10

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         2076262 REVIEW/DT
L12           69 L5 AND REVIEW/DT

=> s l12 and pd < january 2003
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                  (PD<20030100)
L13           14 L12 AND PD < JANUARY 2003

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FILE 'REGISTRY' ENTERED AT 00:17:15 ON 11 OCT 2007

FILE 'HCAPLUS' ENTERED AT 00:17:20 ON 11 OCT 2007

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L1             0 S ANTRANILIC () ACID () AMIDE?
L2            67 S ANTHRANILIC () ACID () AMIDE?
L3             1 S L2 AND VEGF () INHIBITOR?
L4             0 S L3 AND REVIEW/DT
L5           258 S VEGF () INHIBITOR?
L6             1 S L5 AND NEOPLASTIC () DISEASE?
L7            45 S L5 AND RETINOPATHY?
L8            11 S L7 AND REVIEW/DT
L9             0 S L5 AND AGE-RELATED () MACULA () DEGENERATION?
L10           31 S AGE-RELATED () MACULA () DEGENERATION?
L11            0 S L5 AND L10
L12           69 S L5 AND REVIEW/DT
L13           14 S L12 AND PD < JANUARY 2003

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L14            9 L13 NOT L8

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L14  ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:175425  HCAPLUS
DOCUMENT NUMBER:          140:318872
TITLE:                    The role of vascular endothelial growth factor in
                          cerebral edema formation
AUTHOR(S):                Josko, Jadwiga; Knefel, Krzystof
CORPORATE SOURCE:         Chair and Department of Environmental Medicine and
                          Epidemiology, Medical University of Silesia, Zabrze,
                          Pol.
SOURCE:                   Folia Neuropathologica (2003), 41(3),
                          161-166
                          CODEN: FONEEW; ISSN: 1641-4640
PUBLISHER:                Via Medica
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review.  Cerebral edema induced by hypoxia is connected with activity of
     vascular endothelial growth factor (VEGF).  Hypoxia activates VEGF
     expression, which leads to the increase of endothelial permeability.
     Hypoxia-induced VEGF-overexpression is connected with transcriptional
     activation by hypoxia-inducible factor 1 (HIF-1) and posttranscriptional
     stabilization of mRNA by proteins such as HuR.  Also a number of VEGF
     receptors increases in response to hypoxia.  Transcriptional activation by
     HIF-1 (receptor fit-1) and posttranscriptional mechanism (receptor KDR)
     play a key role in this process.  Vascular endothelial growth factor
     increases the permeability and this process is very effective in hypoxia,
     which prevents the rapid autoxidn. of the second messenger NO.  Many
     VEGF inhibitors can be used in future for prevention or
     treatment of hypoxia-induced cerebral edema.  They can inhibit VEGF
     formation (as used in cerebral edema dexamethasone, or barbiturates,
     trichstatin A, candesartan, small mol. inhibitors of hypoxia-inducible
     factor 1, gelandamycin, ribozymes and catechins) or VEGF-activity (soluble
     receptors, monoclonal antibodies, heterodimeric antagonistic VEGF variant,
     RTK inhibitors and catechins).
REFERENCE COUNT:          51    THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14  ANSWER 2 OF 9  HCAPLUS  COPYRIGHT 2007 ACS on STN
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Updated Search

ACCESSION NUMBER: 2003:588122 HCAPLUS
DOCUMENT NUMBER: 139:255461
TITLE: Building a better trap
AUTHOR(S): Hood, John D.; Cheresh, David A.
CORPORATE SOURCE: Department of Immunology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(15), 8624-8625
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review of the treatment of cancer using antiangiogenic agents, especially those that antagonize vascular endothelial growth factor (VEGF). An innovative anti-VEGF therapy coined VEGF-Trap in which Ig domains from the lower-affinity VEGF receptor Flk and the high-affinity VEGF receptor Flt-1 are fused to generate a soluble VEGF inhibitor with favorable pharmacokinetic properties and an extraordinarily high binding affinity is discussed.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:417480 HCAPLUS
DOCUMENT NUMBER: 139:191543
TITLE: The biology of VEGF and its receptors
AUTHOR(S): Ferrara, Napoleone; Gerber, Hans-Peter; LeCouter, Jennifer
CORPORATE SOURCE: Department of Molecular Oncology, Genentech, Inc., South San Francisco, CA, 94080, USA
SOURCE: Nature Medicine (New York, NY, United States) (2003), 9(6), 669-676
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Vascular endothelial growth factor (VEGF) is a key regulator of physiol. angiogenesis during embryogenesis, skeletal growth and reproductive functions. VEGF has also been implicated in pathol. angiogenesis associated with tumors, intraocular neovascular disorders and other conditions. The biol. effects of VEGF are mediated by two receptor tyrosine kinases (RTKs), VEGFR-1 and VEGFR-2, which differ considerably in signaling properties. Non-signaling co-receptors also modulate VEGF RTK signaling. Currently, several VEGF inhibitors are undergoing clin. testing in several malignancies. VEGF inhibition is also being tested as a strategy for the prevention of angiogenesis, vascular leakage and visual loss in age-related macular degeneration.
REFERENCE COUNT: 137 THERE ARE 137 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:124615 HCAPLUS
DOCUMENT NUMBER: 139:223426
TITLE: Pharmacological therapy for age-related macular degeneration. Current developments and perspectives
AUTHOR(S): Holz, F. G.; Miller, D. W.
CORPORATE SOURCE: Univ.-Augenklinik Heidelberg, Heidelberg, 69120, Germany
SOURCE: Ophthalmologe (2003), 100(2), 97-103

Updated Search

CODEN: OHTHEJ; ISSN: 0941-293X
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review. Current therapeutic options for age-related macular degeneration are very limited and are, at best, only capable of slowing visual loss. Because of this an intensive search for prophylactic agents capable of inhibiting the progression of this disease from early into late forms, as well as for new therapeutic approaches was undertaken. While neuroprotective substances are hoped to prevent cellular death in this disease process, multiple substances capable of inhibiting neovascularization, such as VEGF inhibitors, are in clin. trials. Inhibitors of matrix-metalloproteinases (MMP) and chemotherapeutic agents are also being clin. tested as novel therapies for AMD. Other targets include the inhibition of toxic compound formation in lipofuscin granules such as AZ-E. What follows is an overview of different substances and their stages of development in clin. trials.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:20431 HCAPLUS
DOCUMENT NUMBER: 139:143020
TITLE: Antiangiogenic therapy
AUTHOR(S): Konno, Kiroyuki
CORPORATE SOURCE: Second Department of Surgery, Hamamatsu Medical University, Hamamatsu-shi, Shizuoka, 431-3192, Japan
SOURCE: Kan, Tan, Sui (2002), 45(4), 535-543
CODEN: KTSUDO; ISSN: 0389-4991
PUBLISHER: Aku Media
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. Antiangiogenic therapy and the mechanism of angiogenesis inhibitors are reviewed including matrix metalloprotease inhibitors such as MMP-2, MMP-7, and MMP-9, TNP-470, thalidomide, VEGF inhibitors, angiostatin, endostatin, receptor tyrosine kinase inhibitors, and gene therapy.

L14 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:660129 HCAPLUS
DOCUMENT NUMBER: 137:383415
TITLE: Anti-TNFα in the treatment of inflammatory diseases
AUTHOR(S): Paleolog, Ewa
CORPORATE SOURCE: Kennedy Institute of Rheumatology Division, Faculty of Medicine, Imperial College of Science Technology and Medicine, London, UK
SOURCE: Central European Journal of Immunology (2001), 26(3), 140-148
CODEN: CJIMFW; ISSN: 1426-3912
PUBLISHER: Termedia
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Inflammatory musculoskeletal disorders such as rheumatoid arthritis (RA) and osteoarthritis are a common cause of pain and disability. RA, a systemic disease characterized by a chronic inflammation of the synovial lining of joints, is associated with destruction of cartilage and bone. Many pro-inflammatory cytokines including TNFα, chemokines, and growth factors are expressed in diseased joints. Cytokine inhibitors, for example monoclonal anti-TNFα antibody Infliximab, have demonstrated efficacy in clin. trials, and more

recently have been shown to delay joint damage. TNFα blockade, in addition to reducing joint inflammation and leukocyte infiltration, also results in decreased formation of new blood vessels in the synovium. This formation of blood vessels from the pre-existing vasculature (angiogenesis) is essential in maintaining and nourishing the synovial tissue mass. Many endothelial growth factors have been demonstrated in RA, but vascular endothelial growth factor (VEGF) is the most specific mitogen characterized to date. Expression of VEGF is upregulated in many angiogenesis-dependent diseases, including RA. The authors' studies have shown that serum levels of VEGF are elevated in patients with RA, and are reduced following treatment with anti-TNFα antibody. More recently, the authors found that serum VEGF levels at presentation are elevated in patients with early RA, and are able to predict joint destruction. The central role of angiogenesis in RA suggests that suppression of pannus growth could be a beneficial element of anti-arthritic therapy. The authors have reported that VEGF blockade, using a human form of the soluble VEGF receptor Flt-1, reduced disease severity, and synergized with anti-TNFα antibody. Thus, in diseases such as RA, anti-inflammatory treatments such as anti-TNFα might synergize with anti-angiogenic approaches, including VEGF inhibitors, leading to long term benefit.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:226666 HCAPLUS
DOCUMENT NUMBER: 137:210227
TITLE: The role of gemcitabine in the treatment of malignant mesothelioma
AUTHOR(S): Kindler, Hedy Lee; van Meerbeeck, Jan. P.
CORPORATE SOURCE: Section of Hematology/Oncology, University of Chicago, Chicago, IL, USA
SOURCE: Seminars in Oncology (2002), 29(1), 70-76
CODEN: SOLGAV; ISSN: 0093-7754
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Gemcitabine is broadly active in a variety of solid tumors, including malignant mesothelioma. In vitro, gemcitabine demonstrates activity against mesothelioma cell lines. The role of single-agent gemcitabine in patients with mesothelioma is unclear, since three phase II trials treated a total of 60 patients and achieved response rates of 0%,7%, and 31%. The combination of gemcitabine and cispatin is synergistic against mesothelioma cell lines in vitro. Gemcitabine in combination with cisplatin or carboplatin shows definite activity in phase II trials. The trial by Byrne and colleagues that demonstrated a response rate of 48% established the combination of gemcitabine plus cisplatin as a standard therapy for this disease in the United States. Subsequent multicenter trials have achieved lower response rates of 26% and 16% for this combination. Gemcitabine plus carboplatin also has activity. Future roles for gemcitabine in malignant mesothelioma patients include incorporating a gemcitabine/platinum regimen for neoadjuvant or adjuvant therapy, combining it with other cytotoxic chemotherapy agents such as pemetrexed or vinorelbine, or adding novel cytostatic agents such as the vascular endothelial growth factor (VEGF) inhibitor, bevacizumab, to the gemcitabine and platinating agent combination.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:835175 HCAPLUS

Updated Search

DOCUMENT NUMBER: 137:56717
TITLE: Molecular therapy for multiple myeloma
AUTHOR(S): Martinelli, Giovanni; Tosi, Patrizia; Ottaviani, Emanuela; Soverini, Simona; Tura, Sante
CORPORATE SOURCE: Institute of Hematology and Medical Oncology Seragnoli, University of Bologna, Bologna, 40138, Italy
SOURCE: Haematologica (2001), 86(9), 908-917
CODEN: HAEMAX; ISSN: 0390-6078
PUBLISHER: Ferrata Storti Foundation
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Background and Objectives. Several mol. and cytogenetic advances have suggested novel therapeutic strategies that could help reach an eventual cure for multiple myeloma (MM). Evidence and Information Sources. Identification of novel, MM-specific mol. targets should pave the way for drugs that can specifically attack the neoplastic cells while sparing the normal ones. Drugs that alter the marrow microenvironment - such as bisphosphonates, proteasome inhibitors (e.g. PS-341/LDP341), lactacystin or LLNV compds. - induce apoptosis or G1 growth arrest and alter the adhesion of MM cells to marrow stroma. These drugs that modify the microenvironment have a more solid scientific basis and may, therefore, have more realistic implications in MM treatment. Of these, novel vascular endothelial growth factor (VEGF) inhibitors, such as SU5416 and SU6668, block tumor-cell adhesion and could disrupt MM cell proliferation. Similarly, tyrosine kinase inhibitors (TKI) such as fibroblast growth factor receptor (FGFR) inhibitors, may serve when the FGFR3 gene is overexpressed due to the t(4;14)(p16.3;q32) and/or is activated by point mutations. In cases carrying the translocation and expressing the IgH/WHSC1-MMSET hybrid transcripts, histone deacetylase (HDAC) inhibitors could be useful, but their possible clin. use needs to be supported by more biol. studies. Tumor necrosis factor α-related apoptosis-inducing ligand (TRAIL) induces apoptosis in MM cell lines and primary cells. The proliferative signaling pathway of FGFR3 is mediated by Ras (Ras-activating mutations are frequently found in MM), which presents a possible target for farnesyltransferase inhibitors (used alone or in association with IFN-α). Perspectives. In several of these options, preclin. studies have proved encouraging, and clin. trials are now getting underway.
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:785330 HCAPLUS
DOCUMENT NUMBER: 136:132460
TITLE: Biologic and clinical implications of vascular endothelial growth factor expression in ovarian cancer
AUTHOR(S): Berkenblit, Anna; Cannistra, Stephen A.
CORPORATE SOURCE: Division of Hematology/Oncology, Program in Gynecologic Medical Oncology, Beth Israel Deaconess Medical Center, Boston, MA, 02215, USA
SOURCE: Women's Oncology Review (2001), 1(3), 217-224
CODEN: WOROAR; ISSN: 1473-3404
PUBLISHER: Parthenon Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review on the central role of vascular endothelial growth factor (VEGF) in ovarian cancer and novel therapeutic strategies designed to inhibit its effect on tumor growth. Several lines of evidence suggest a causal link between tumor secretion of VEGF and ascites formation. Vascular

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permeability factor (VPF) and VEGF may play a central role in the formation of ascites by stimulating both angiogenesis and vascular permeability. In preclin. models VEGF inhibitors block the formation of ascites, a therapeutic effect that may be particularly relevant for the treatment of ovarian cancer. Several pharmaceutical agents that block VEGF activity are already being tested in clin. trials in a variety of cancer.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT